

**WHAT IS CLAIMED IS:**

1. An isolated nucleic acid comprising a human PRKAG3 sequence, wherein said human PRKAG3 sequence comprises a nucleotide sequence variant and nucleotides flanking said sequence variant, and wherein said isolated nucleic acid is at least 15 base pairs in length.
2. The nucleic acid of claim 1, wherein said nucleotide sequence variant is associated with a metabolic disease.
3. The nucleic acid of claim 2, wherein said metabolic disease is diabetes or obesity.
4. The nucleic acid of claim 1, wherein said nucleotide sequence variant is in an exon.
5. The nucleic acid of claim 4, wherein said exon is selected from the group consisting of exon 3, exon 4, and exon 10.
6. The nucleic acid of claim 4, wherein said exon 3 variant comprises a substitution of a guanine for a cytosine at nucleotide 230.
7. The nucleic acid of claim 4, wherein said exon 4 variant comprises a substitution of a thymine for a cytosine at nucleotide 550.
8. The nucleic acid of claim 4, wherein said exon 10 variant comprises a substitution of a thymine for a cytosine at nucleotide 1037.
9. The nucleic acid of claim 1, wherein said nucleotide sequence variant is in an intron.
10. The nucleic acid of claim 9, wherein said nucleotide sequence variant is in intron 6.

11. The nucleic acid of claim 1, wherein said PRKAG3 nucleic acid sequence encodes an AMP-activated protein kinase  $\gamma 3$  subunit polypeptide, said polypeptide comprising an amino acid sequence variant.
12. The nucleic acid of claim 11, wherein said amino acid sequence variant comprises substitution of an alanine residue for a proline residue at amino acid 71.
13. The nucleic acid of claim 11, wherein said amino acid sequence variant comprises substitution of a tryptophan residue for an arginine residue at amino acid 340.
14. A method for determining a risk estimate of a metabolic disease in a subject, said method comprising detecting the presence or absence of a PRKAG3 nucleotide sequence variant in said subject, and determining said risk estimate based, at least in part, on presence or absence of said variant in said subject.
15. The method of claim 14, wherein said metabolic disease is diabetes or obesity.
16. A method for detecting a PRKAG3 polypeptide variant in a subject, said method comprising providing a biological sample from said subject, contacting said biological sample with an antibody having specific binding affinity for said PRKAG3 polypeptide variant, and detecting the presence or absence of said PRKAG3 polypeptide variant in said biological sample.
17. An article of manufacture comprising a substrate and an array of different nucleic acids immobilized on said substrate, wherein at least one of said different nucleic acids is a PRKAG3 nucleic acid, and wherein said PRKAG3 nucleic acid comprises a PRKAG3 nucleotide sequence variant and nucleotides flanking said sequence variant.
18. The article of manufacture of claim 17, wherein said array comprises multiple PRKAG3 nucleic acids, wherein each of said PRKAG3 nucleic acids comprises a different PRKAG3 nucleotide sequence variant and nucleotides flanking said sequence variant.